

Amendments to the Claims:

1. (Cancelled)
2. (Cancelled)
3. (Cancelled)
4. (Currently amended) ~~The An antibody fragment of claim 2 comprising a Fab' fragment that has been modified by replacement of the interchain cysteine of C_H1 with another amino acid and wherein the C_L interchain cysteine is covalently bonded to a cysteine in the hinge region, and wherein the hinge region is modified to comprise SEQ ID NO: 1 or SEQ ID NO: 2.~~
5. (Previously presented) An antibody Fab' fragment in which both the interchain cysteine of C_H1 and the interchain cysteine of C_L have been replaced by another amino acid and an engineered cysteine in the light chain constant region is covalently bonded to a cysteine in the hinge region.
6. (Previously presented) The antibody fragment of claim 5 wherein the light chain constant region comprises any one of the sequences provided in the SEQ ID Nos 16-20.
7. (Previously presented) The antibody fragment of claim 6 wherein the hinge region comprises any one of the sequences provided in SEQ ID Nos 1-11.
8. (Cancelled)
9. (Cancelled)
10. (Cancelled)
11. (Cancelled)
12. (Cancelled)

13. (Cancelled)

14. (Currently amended) An antibody Fab or Fab' fragment that has been modified by replacement of either the interchain cysteine of C_H1 or the interchain cysteine of C_L with another amino acid ~~The Antibody fragment of claim 1 wherein at least two effector molecules are attached to the fragment, each of said effector molecules being PEG or a derivative thereof.~~

15. (Currently Amended) The antibody fragment of claim 14 wherein one of said an effector molecule molecules is attached to ~~a~~ an engineered cysteine in the light chain constant region and/or to ~~a~~ an engineered cysteine in the heavy chain constant region.

16. (Cancelled)

17. (Currently amended) The antibody fragment of claim 14 wherein one of said an effector molecules molecule is attached to the interchain cysteine of C_L, to the interchain cysteine of C_H1, or to an engineered cysteine in the light chain constant region.

18. (Currently amended) The antibody fragment of claim + 14 wherein the fragment is a Fab' fragment in which one of said an effector molecules molecule is attached to each cysteine in the hinge region.

19. (Currently amended) The antibody fragment of claim 18 wherein one of said an effector molecules molecule is attached to a cysteine in the hinge region that was covalently linked to the interchain cysteine of C_L prior to attachment of the effector molecules.

20. (Currently amended) The antibody fragment of claim 18 wherein one of said an effector molecules molecule is attached to a cysteine in the hinge region that was covalently linked to an engineered cysteine in the light chain constant region prior to attachment of the effector molecules.

21. (Withdrawn) A method of producing an antibody fragment of claim 14 comprising:

- a. treating an antibody Fab or Fab' fragment in which either the interchain cysteine of C_H1 or the interchain cysteine of C_L has been replaced by another amino acid with a reducing agent capable of generating a free thiol group in at least one cysteine of the heavy and/or light chain constant region and/or, where present, the hinge; and
- b. reacting the treated fragment with an effector molecule.

22. (Withdrawn) The method of claim 21 wherein step (a) further comprises reducing the covalent bond between the C_L interchain cysteine and a cysteine in the hinge region.

23. (Withdrawn) The method of claim 21 wherein step (a) further comprises reducing the covalent bond between an engineered cysteine in the light chain constant region and a cysteine in the hinge region.

24. (Currently amended) An antibody fragment comprising a Fab or Fab' fragment that has been modified by attachment of two or more effector molecules wherein the heavy chain in the fragment is not covalently bonded to the light chain, and an effector molecule is attached to each of the interchain cysteines of C_L and C_H1, and wherein at least two effector molecules are PEG or a derivative thereof.

25. (Previously presented) The antibody fragment of claim 24 wherein at least one further effector molecule is attached to a cysteine in the light chain constant region and/or to a cysteine in the heavy chain constant region.

26. (Previously presented) The antibody fragment of claim 25, wherein an effector molecule is attached to a cysteine in the light chain constant region and to a cysteine in the heavy chain constant region, and the two cysteines would otherwise be linked to each other via a disulphide bond if the effector molecules were not attached.

27. (Currently amended) The antibody fragment of claim 2624 wherein the fragment is a Fab' fragment that contains a modified hinge region.

28. (Previously presented) The antibody fragment of claim 27 wherein the hinge region comprises any one of the sequences provided in SEQ ID Nos 1-14.

29. (Previously presented) The antibody fragment of claim 24 wherein the fragment is a Fab' fragment and an effector molecule is attached to at least one cysteine in the hinge region.

30. (Withdrawn) A method of producing an antibody fragment of claim 24 comprising:

- a. treating an antibody Fab or Fab' fragment with a reducing agent capable of generating a free thiol group in at least the interchain cysteine of C_H1 and the interchain cysteine of C_L; and
- b. reacting the treatment fragment with an effector molecule.

31. (Withdrawn) The antibody fragment of claims 1 or 24 wherein the interchain cysteine of C_L is at position 214 of the light chain and the interchain cysteine of C_H1 is at position 233 of the heavy chain.

32. (Withdrawn) The method of claims 21 or 30 wherein the reducing agent is a non-thiol based reducing agent.

33. (Withdrawn) The method of claim 32 wherein the reducing agent is a trialkyphosphine.

34. (Withdrawn) The method of claim 33 wherein the trialkyphosphine reducing agent is tris(2-carboxyethyl)phosphine (TCEP).

35. (Withdrawn) The method of claim 33 wherein the trialkylphosphine reducing agent is tris(3-hydroxypropyl)phosphine (THP).

36. (Withdrawn) The method of claim 21 wherein either or both of steps (a) and (b) are performed in the presence of a chelating agent.

37. (Withdrawn) The method of claim 36 wherein the chelating agent is EDTA.

38. (Withdrawn) The method of claim 37 wherein both steps (a) and (b) are performed in the presence of EDTA.

39. (Cancelled)

40. (Cancelled)

41. (Currently amended) The antibody fragment of claim claims 14 or 24 wherein the each effector molecule is PEG or a derivative thereof.

42. (Cancelled)

43. (Currently amended) A pharmaceutical composition comprising an antibody fragment of claims-1 claim 14 or 24, together with one or more pharmaceutically acceptable excipients, diluents or carriers.

44. (Cancelled)